

### REMARKS

Reconsideration of the application, as amended, is respectfully requested.

The term "health active" has been replaced with the term more widely used in the art, "probiotics." The definition on page 6, lines 1-2 of the description supports this. No surrender of subject matter is intended.

The same amendment has been made to independent claims 9, 10, 11 and 13.

The term "probiotic" is well known in the art as can be seen from the enclosed reference Probiotics by F. Guarner and G.S. Schaafsma published by International Journal of Food Microbiology 39(1998) 237-238.

Since the Office is of the view that sweets encompasses chewing gum, ice cream, chocolate and bars, these have been placed in dependent claims claim 6 and 19.

New claim 23 has been added to recite that the cereal food product of claim 6 is a bar. The Examiner is rejecting claims as being anticipated by Hutkins et al. (US 5,186,962). It is thus noticed that claim 9 is still allowed.

The present invention, as defined in all claims, recites a non-viable probiotic Lactobacillus bacteria (in the method and in the food composition). Hutkins et al., however, have a viable bacteria present and make no teaching or suggestion to use a non-viable bacteria.

The probiotic Lactobacillus bacteria according to the present invention are non-viable bacteria. From the definition on page 5, lines 14 to 17 of the present description, this

means that "substantially all or all bacteria" are not capable of growing under the appropriate growing conditions of said Lactobacillus strain.

Thus, the present invention utilizes probiotic Lactobacillus bacteria which are not capable of growing even under suitable growing conditions. If the Lactobacillus bacteria of the present invention were placed in favorable growing conditions for that type of bacteria, they simply cannot grow (or multiply). This is what is meant by non-viable.

In summary, the Lactobacillus bacteria according to the present invention are non-living (non-metabolically active) non-growing bacteria under all conditions.

The bacteria of Hutkins et al., cited by the Office, are viable bacteria. From the definition on page 5, lines 10-12 of the present description, viable Lactobacillus bacteria according to the present invention are those which "are capable of growing under the appropriate growing conditions of said Lactobacillus strain."

Hutkins et al. use Lactobacillus bacteria which are capable by growing under suitable growing conditions as supported by the reasons given below:

- Hutkins et al. control the conditions in the food product so that the Lactobacillus bacteria are unable to grow/multiply even though they are still living (see col. 3 line 44 – col. 4 line 18). The conditions in the food product are controlled so that the bacteria do not grow or ferment. This may be achieved by refrigerating the food or by using other substances in the food product that inhibit cell growth of the bacteria (col. 4 lines 5/6 – col. 5 line 3). However, they are still alive within the food product. If the conditions in the food product were changed, e.g. the food was diluted, the cell growth inhibiting substances were omitted, refrigeration was not used, or if the bacteria were taken out of the food and placed in suitable growth conditions the

bacteria would begin to grow/ferment again because they are living, metabolically active bacteria which are capable of growing/fermenting under suitable conditions. Thus the bacteria of Hutkins et al. are viable according to the definition of the present invention.

- Alternatively, Hutkins et al. use a non-fermentative bacteria which is incapable of significantly fermenting a nutrient, carbohydrate such as glucose, lactose, sucrose, raffinose, xylose and the like and/or other substance which is contained in the food substance and required for fermentation, as for example, a vitamin and the like (col. 4 lines 30-45). Thus, these bacteria of Hutkins cannot use the nutrients, which are present in the food product to grow/ferment. However, if these bacteria were placed in suitable conditions with a nutrient which they could ferment, then growth/fermentation would occur. Thus, these bacteria of Hutkins et al. are alive and viable.
- Thus Hutkins et al. disclose living bacteria that are stopped from growing/fermenting because of the conditions in which they are kept, but, that when put into suitable growing conditions would begin to grow/ferment because they remain metabolically active. In col. 5, line 55 +, Hutkins et al. disclose that the cell count or concentration of bacteria when added to the food product does not increase by more than 10-100%, preferably about 10-50%, within the food mixture. Accordingly, to be able to increase in numbers, the bacteria of Hutkins et al. must be living bacteria which are capable of growing under appropriate conditions and which are thus viable according to the present invention.

### Summary

1) bacteria of the present invention are non-living bacteria which are not capable of growth/fermentation under suitable growing conditions i.e. non-viable.

2) bacteria of Hutkins et al. are living bacteria which are capable of growth/fermentation under suitable growing conditions i.e. viable.

FAX RECEIVED

JUN 17 2003


GROUP 1700

Accordingly, the present invention is novel over the disclosure of Hutkins et al. as the Lactobacillus bacteria are in a completely different physical state. Furthermore, there is no teaching by Hutkins that the benefits of the present invention can be achieved by using non-viable bacteria.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings To Show Changes Made.**"

In view of the foregoing, it is respectfully requested that the application, as amended, be allowed.

Respectfully submitted,



Gerard J. McGowan, Jr.  
Attorney for Applicant(s)  
Reg. No. 29,412

GJM:pod  
(201) 840-2297

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Please amend claims 1, 6, 9, 10, 11 and 19, as follows:

In the claims:

1. (Twice amended) A method to produce a food product comprising health ~~active~~probiotic Lactobacillus bacteria which have been rendered non-viable ~~Lactobacillus bacteria~~, wherein the method comprises the step of adding said probiotic Lactobacillus bacteria as non-viable Lactobacillus bacteria into the food product, and wherein no substantial fermentation of the food product by said Lactobacillus bacteria will take place.
6. (Twice Amended) Method according to claim 1 wherein the food product is selected from the group consisting of soups, noodles, ~~ice-cream, sauces, dressing, spreads, snacks, cereals, beverages, bread, biscuits, [other bakery products], sweets, bars, chocolate, chewing gum, dairy products, dietetic products, and~~ dietetic products.
9. (Twice amended) A food product having a pH of 3.8 or less, said food product comprising health ~~active~~probiotic Lactobacillus bacteria which have been rendered non-viable ~~Lactobacillus bacteria~~ and said food product being substantially non-fermented by said Lactobacillus bacteria.
10. (Twice amended) A food product having a pH of 5.0 or more, said food product comprising health ~~active~~probiotic Lactobacillus bacteria which have been rendered non-viable ~~Lactobacillus bacteria~~ and said food product being substantially non-fermented by said Lactobacillus bacteria.

11. (Twice amended) A food product having an  $A_w$  of 0.90 or less, said food product comprising ~~health-active~~ probiotic Lactobacillus bacteria which have been rendered non-viable ~~Lactobacillus bacteria~~ and said food product being substantially non-fermented by said Lactobacillus bacteria.

19. (Amended) Method according to claim 14 wherein the food product is selected from the group consisting soups, noodles, [ice-cream,] sauces, dressing, spreads, [snacks,] cereals, beverages, bread, biscuits, [other bakery products,] sweets, [bars,] [chocolate, chewing gum,] dairy products, and dietetic products.



## Short communication Probiotics

F. Guarner<sup>a,\*</sup>, G.J. Schaafsma<sup>b</sup>

for LABIP Workshop participants<sup>1</sup>, <sup>a</sup>Digestive System Research Unit, Hospital General Vall d'Hebron, 08035 Barcelona, Spain  
<sup>b</sup>TNO Nutrition and Food Research Institute, 3700 AZ Zeist, Netherlands

Received 25 November 1997; accepted 27 November 1997

There is currently a growing interest in certain lactic acid bacteria strains that have been suggested or shown to provide specific health benefits when consumed as food supplements or as food components. However, opinions differ widely with respect to the requirements needed to substantiate a claim on a beneficial effect of a given bacterial strain, and there is no consensus on how to define and accredit a viable strain as a probiotic. On the other hand, putative risks of massive introduction of new live microorganisms in nutrition should also be envisaged, even if benefits were proven. The Lactic Acid Bacteria Industrial Platform (LABIP)<sup>2</sup> hosted a

workshop sponsored by the European Community to discuss these topics<sup>3</sup>.

Firstly, the workshop issued a consensus definition of probiotics: "oral probiotics are living micro-organisms, which upon ingestion in certain numbers, exert health benefits beyond inherent basic nutrition". According to the new definition, probiotics may be consumed either as a food component or as a non-food preparation.

For the demonstration of probiotic activity of a certain strain, the group concluded that well-designed human studies (double blinded, placebo-controlled) are required. Several *in vitro* assays or animal studies such as tests on resistance to bile and acid, adhesion to the intestinal mucosa, effects on immunocompetent cells or antimutagenicity, are very useful in the preselection of bacterial strains. However, the proof of efficacy in humans should be granted by at least one well-designed human study. Preferentially, the study should be published in a peer-reviewed journal.

Based on these criteria, the group discussed and proposed to make a distinction between established beneficial effects of probiotics, and potential benefits that need further substantiation. For instance, several lines of evidence have established the benefits of

\*Corresponding author.

<sup>1</sup>List of LABIP Workshop participants: Dr. W. Boersma (Leiden, Netherlands), Prof. J.K. Collins (Cork, Ireland), Dr. M. Coste (Jouy-en-Josas, France), Dr. I. de Smet (Gent, Belgium), Dr. F. Guarner (Barcelona, Spain), Prof. W. Hammes (Stuttgart, Germany), Dr. T. Matilla-Sandholm (Helsinki, Finland), Prof. L. Morelli (Piacenza, Italy), Dr. B.L. Pool-Zobel (Karlsruhe, Germany), Dr. I.R. Rowland (London, UK), Prof. G.J. Schaafsma (Zeist, Netherlands), Prof. K.H. Schleifer (München, Germany), Dr. M. Tvede (Viborg, Denmark), Prof. T. Wadstrom (Lund, Sweden), Dr. B. Weile (Gentofte, Denmark). Chairman: Dr. J.W. vd Kamp (Zeist, Netherlands). EU-representative: Dr. A. Aguilar (Brussels, Belgium).

<sup>2</sup>LABIP is an European Economical Association of companies involved in the use and production of lactic acid bacteria (LAB). Its goals are to promote R and D on LAB within the EU and to develop an opinion on research needs for LAB within the EU.

<sup>3</sup>The Workshop on Probiotics was held in Frankfurt (Germany) from 13 to 15 November 1995.

certain probiotics to reduce signs and symptoms of lactose intolerance (Sanders, 1993), prevention and treatment of certain diarrhoeal diseases (Biller et al., 1995; Kaila et al., 1995; Majamaa et al., 1995; Saavedra et al., 1994; Siitonen et al., 1990), reduction of bacterial enzyme activities (Sanders, 1993) and stimulation of the immune system (De Simone et al., 1993; Schiffrin et al., 1995). Potential benefits of the ingestion of probiotics can also be expected in other important fields such as modulation of blood cholesterol levels, competitive exclusion of intestinal pathogens, and cancer prevention.

The unlimited use of probiotics might have unwanted side-effects. Most likely, these effects would not affect the normal healthy population, but should be considered when used by specific subgroups of persons 'at risk'. For instance, infection and toxicity by probiotics has never been documented, but subjects with underlying disease conditions that predispose to infection might be exposed to a putative risk (Adams and Marteau, 1995). Likewise, unrestricted stimulation of the immune system by probiotics could be detrimental for patients suffering autoimmune diseases. The risk of transfer of antibiotic resistance properties from probiotics to virulent micro-organisms should also be evaluated.

Studies on probiotics that will reasonably expand our knowledge in this emerging field should be encouraged for active research in forthcoming years.

A copy of the full report of the Workshop is available from the participants.

## References

- Adams, M.R., Marteau, P., 1995. On the safety of lactic acid bacteria from food. *Int J Food Microbiol* 27, 263–264.
- Biller, J.A., Katz, A.J., Flores, A.F., Buie, T.M., Gorbach, S.L., 1995. Treatment of recurrent *Clostridium difficile* colitis with *Lactobacillus* GG. *J Pediatr Gastroenterol* 21, 224–226.
- De Simone, C., Vesely, R., Bianchi Salvadori, B., Jirillo, E., 1993. The role of probiotics in modulation of the immune system in man and in animals. *Int J Immunotherapy* IX, 23–28.
- Kaila, M., Isolauri, E., Saxelin, M., Arvilommi, H., Vesikari, T., 1995. Viable versus inactivated *Lactobacillus* strain GG in acute rotavirus diarrhoea. *Arch Dis Child* 72, 51–53.
- Majamaa, H., Isolauri, E., Saxelin, M., Vesikari, T., 1995. Lactic acid bacteria in the treatment of acute rotavirus gastroenteritis. *J Pediatr Gastroenterol Nutr* 20, 333–338.
- Saavedra, J.M., Bauman, N.A., Oung, I., Ferman, J.A., Yolken, R.H., 1994. Feeding of *Bifidobacterium bifidum* and *Streptococcus thermophilus* to infants in hospital for prevention of diarrhoea and shedding of rotavirus. *Lancet* 334, 1046–1049.
- Sanders, M.E., 1993. Summary of conclusions from a consensus panel of experts on health attributes of lactic cultures: significance to fluid milk products containing cultures. *J Dairy Sci* 76, 1819–1828.
- Schiffrin, E., Rochat, F., Link-Amster, H., Aeschlimann, J., Donnet-Hugues, A., 1995. Immunomodulation of blood cells following the ingestion of lactic acid bacteria. *J Dairy Sci* 78, 491–497.
- Siitonen, S., Vapaatalo, H., Salminen, S. et al., 1990. Effect of *Lactobacillus* GG yoghurt in prevention of antibiotic associated diarrhoea. *Ann Med* 22, 57–59.